UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,590	12/14/2001	Jukka Salonen	0933-0179P	2024

2292 7590 06/18/2003

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	8

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/014,590	Applicant(s) SALONEN, JUKKA	
	Examin r San-ming Hui	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the invention of Group II, claims 13-23 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that no undue burden would be imposed to the Office since the kits and the method recited herein involved related technical features. This is not found persuasive because the method of treating an individual for reducing cardiovascular risk and the kit for diagnostic method are classified in different classifications. Since the different inventions fall into different classifications, the field of search is diverse as they are recognized to be in separate states of art. See MPEP § 808.02(c). The search is not limited to patent files. Therefore, the search for all the different inventions herein would present an undue burden to the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-12 and 24-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Claims 13-23 have been examined herein to the extent they read on the elected invention, insofar as they are not related to gene therapy.

Claim Objections

Claim 19 is objected to because of the following informalities: the use of parenthesis in claim 19, last line: "(ATP-binding cassette A1)", is considered improper. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for testing liver damage and oxidative stress associated with paraoxonase activity, does not reasonably provide enablement for other disorders that detrimentally affects the protective effect of HDL. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

The instant claims are very board. They encompass all disorders that detrimentally affect the protective effect of HDL; however, Applicant fails to set forth the criteria that define such disorder. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these disorders without undue experimentation. In the instant case, only a limited number of "disorders that detrimentally affect the protective effect of HDL" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the disorders recited. In Navab et al. (Arterioscler Thromb Vasc. Biol., 1996;16(7):831-842), it teaches that certain genetic factors also contribute to the oxidative functions of HDL or the lack thereof. One of the disorders might be the overexpression of inflammatory genes in the liver that impairs the antioxidative function of HDL (See page 838, col. 1). Without providing guidance as to the method of ascertaining such conditions, one of skilled in the art would have to perform undue experimentation to identify such individual. It Is apparent that identifying such individual is highly unlikely or unpredictable, requiring each embodiment to be individually assessed, since there are so many factors could potentially affect the oxidative capacity of HDL. Applicants fail to

provide information sufficient to practice the claimed invention, absent undue experimentation.

Claims 13-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the claims herein encompass the protection for the risk of all cardiovascular diseases. The term "Protect" means "to keep from harm, attack, or injury" (See Webster's II New Riverside University Dictionary, 1984, page 946). When such term is recited in the instant claims, it means absolute protection against the risk of all cardiovascular diseases. It is known in the art that the etiology of primary hypertension is unknown (See Merck Manual, 16th ed., 1992, page 413). Therefore, it is almost impossible, if not unlikely, to diminish the risk of getting hypertension to zero (i.e., the absolute protection). Moreover, cardiovascular diseases can be caused by offending agents such as viruses, which are not related to functions of HDL (See Fields Virology, 3rd ed., published by Lippincott-Raven, 1996, page 673-675). Therefore, it is very unlikely the instant recited method would be effective in absolute protecting an individual against the risk of cardiovascular disorders that are viral originated. The instant specification fails to provide sufficient information to enable one of skilled in the art practicing the instant invention.

Claims 13, 14, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). In the instant case, the specification fails to describe the genotyping mutations or polymorphisms that will influence serum or plasma γ-glutamyltransferase activity or concentration, or mutations in the phase I and II enzymes or the expression thereof. In the specification, page 5, line 17-29, it merely describes commonly known techniques to genotype DNA from blood sample. However, there is no description in the specification as to the specific mutation or polymorphism that will produce the activities or effects as recited in the claim. Examiner notes that such specific mutations and/or polymorphisms are important

to the functions claimed (i.e., influencing the serum or plasma γ-glutamyltransferase activity or concentration, or mutations in the phase I and II enzymes or the expression thereof). Examiner further notes that the claim encompasses a wide array of molecules with different sequences. The specification does not disclose any of these variants, modifications or mutants, nor does it provide any teachings as to how the structures of these sequences relate to their function. Thus, the specification does not describe the complete structure of a representative number of species. Neither does the specification describe a representative number of species in terms of partial structure and relevant identifying characteristics. Absent of such teachings and guidance as to the structure-function relationship of these molecules, the specification does not describe the claimed molecules and the use thereof in such full, clear, concise and exact terms so as to indicate that Applicant had possession of these molecules and the use thereof at the time of filing of the present application. Thus, the written description requirement has not been satisfied.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "detrimentally" in claim 13 is a relative term which renders the claim indefinite. The term "detrimentally" is not defined by the claim, the specification does

not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what degree of protective effect of HDL would be considered "detrimentally" impaired. For example, is the protective effect of HDL considered detrimental when it is totally diminished? Or only 95% diminished?

The expression "treating the selected individual ... enhance the HDL or HDL cholesterol level" recited in claim 13 renders the claim indefinite as to the exact method encompassed by the claims. It is not clear what treatment method are the claims encompassed for achieving the end results of enhance the HDL or HDL cholesterol level. Would the enhancement of the HDL or HDL cholesterol level be achieved by medicament alone? by diet alone? or by the combination of both?

The phrase "these genes" recited in claim 16 renders the claim indefinite as to what genes it is referred to.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the

claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 19 recites the broad recitation "sterol absorption inhibiting agent", and the claim also recites "a resin, ..., a ABCI agonist" which is the narrower statement of the range/limitation. In claim 19 also recites the broad recitation "PPAR agonist", and the claim also recites "fibrate" which is the narrower statement of the range/limitation.

Claim 19 contains the trademark/trade name "a CETP inhibitor, an ACAT inhibitor, a PLTP agonist, a LCAT agonist, a LPL agonist, a SR-B1 agonist, or a ABC1 agonist". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe treatment for enhancing HDL level and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-14 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Facts (Drug Facts and Comparisons, 1999, page 1082-1092, 1100).

Facts teaches gemfibrozil is useful to reduce coronary heart disease risk and also patients with hepatic dysfunction (liver damage) should not take gemfibrozil (See page 1100). Facts also teaches that HMG-CoA reductase inhibitor, pravastatin is known to reduce the risk of myocardial infarction (See page 1092). Facts also teaches that one of the contraindications of HMG-CoA reductase inhibitors is acute liver disease (i.e., liver damages) or unexplained persisent elevated liver function tests (See page 1084). The testing for liver damage would be inherent in the method since clinicians would need to avoid patients with liver damage when prescribing the drugs.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-15, 17-19, and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lyons et al. (British Journal of Clinical Pharmacology, 1994;37:59-62) and Merck Manual (16th ed., page 408-412) in view of Boden (American Journal of Cardiology, 2000;86:12:19-22L), Navab et al., Traub (Basic Skills in Interpreting Laboratory Data, chapter 9, page 121-129), and Applicant's admission, insofar as they related to the reduction of risk of cardiovascular disease.

Lyons et al. teaches colestipol can enhance the HDL level (See abstract).

Merck Manual teaches that regular exercise can increase the HDL level (See page 412).

The references do not expressly teach the increase of HDL levels can reduce the risk of heart disease. The references do not expressly teach the testing method recited herein for checking the paraoxonase level, γ-glutamyl transferase (GGT) level and HDL oxidative capacity. The references do not expressly teach the exclusion of individual having the disorders that affects the protective effect of HDL.

Boden teaches that HDL is one of the most significant risk factor for coronary artery disease with the increase of 1% of HDL resulting a 3% decrease of risk of heart disease (See the abstract; also page 21L-22L).

Navab et al. teaches the antioxidant effect of HDl is depending on paraoxonase and PAF acetylhydrolase (See page 835, col. 2 to page 837, col. 2; especially Fig.2 on page 836). Navab et al. also teaches that in certain conditions such as the acute phase response, the paraoxonase and PAF acetylhydrolase activities are reduced significantly even though the HDL level remains (See page 837, col. 1).

Traub teaches testing GGT level is known for checking the liver functions and damages (See page 127, col. 1-2). Traub also teaches that a marked elevated level of GGT might indicate alcoholic liver disease (See page 127, col. 1, last three paragraphs).

Applicant's admission, citing the article of Perova et al., that for heavy ethanol drinkers, high plasma HDL levels does not associate with reduced coronary and total mortality (See page 1, lines 24-27 of the instant specification, Background of the invention Section).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ colestipol or exercise in patients who is having alcoholic liver disease (i.e., having elevated GGT level) to reduce the risk of heart disease.

One of ordinary skill in the art would have been motivated to employ colestipol in patients who is having alcoholic liver disease (i.e., having elevated GGT level) to reduce the risk of heart disease since both exercise and colestipol are known to enhance the

HDL levels, which can decrease the risk of heart disease. Therefore, treating patients that are free from alcoholic liver diseases for the reduction of risk in heart disease would be reasonably expected to be beneficial. Moreover, excluding the patients with low paraoxonase activity from the HDL enhancing treatment would be reasonable and obvious since the antioxidative protecting effect of HDL is depending on the level of paraoxonase. The method of reduction of risk of heart disease would be reasonably be expected to be effective in patients with high HDL levels as well as high paraoxonase level.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
Patent Examiner
Art Unit 1617
June 16, 2003